CHEK2 Biallelic gene

Associated Syndrome Name: *CHEK2*-associated cancer risk (biallelic)

CHEK2 Biallelic Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Breast	High Risk
Male Breast	Elevated Risk
Prostate	Elevated Risk

CHEK2 Biallelic gene Overview

CHEK2-associated cancer risk (biallelic) [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13]

- Women with mutations in both copies of the *CHEK2* gene (biallelic mutations) have a risk for breast cancer that is significantly increased over the 12.5% lifetime risk for women in the general population of the United States. This risk is also significantly higher than the breast cancer risk for women with a mutation in only one copy of the *CHEK2* gene (monoallelic mutation).
- Men with *CHEK2* mutations also have an increased risk for breast cancer. The estimates provided in the following table are based on studies of men with a single *CHEK2* mutation. The risks for men with biallelic *CHEK2* mutations may be higher.
- It is not known if there are additional cancer risks for men and women with mutations in both copies of the *CHEK2* gene. Some studies have described a possible increased risk for a wide range of cancers in patients with a single *CHEK2* mutation, including gastric, thyroid, renal, hematological malignancies, testicular germ cell tumors, and other malignancies. However, these studies are not conclusive and there are currently no medical management guidelines to address these possible risks.
- Although there are increased risks for cancer in men and women with mutations in *CHEK2*, there are interventions that may reduce these risks. Guidelines from the National Comprehensive Cancer Network (NCCN) that may apply are listed below. These guidelines were developed for men and women with a mutation in only one copy of the *CHEK2* gene. It may be appropriate to modify these recommendations based on the possibility of higher cancer risks in patients with mutations in both copies of the *CHEK2* gene. Since information about the cancer risks associated with biallelic *CHEK2* mutations is relatively new, and there is still some uncertainty about the best ways to reduce these risks, it may be appropriate to interpret these results in consultation with cancer genetics experts in this emerging area of knowledge.

CHEK2 Biallelic gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Female Breast	To age 80 [1, 14]	Up to 89%	10.8%
	Second primary within 10 years of first breast cancer diagnosis [12, 15, 16, 17]	7%-29%, or higher	3.5%
Male Breast	To age 80 [4, 14, 18]	0.4%-1%, or higher	0.1%
Prostate	To age 80 [19, 20]	Elevated risk	10.9%

CHEK2 Biallelic Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Female Breast	The recommendations below were developed for women with a single *CHEK2* mutation. Currently there are no specific management recommendations for breast cancer risk in women with biallelic *CHEK2* mutations. However, the increased risk for breast cancer in biallelic carriers compared to monoallelic carriers warrants consideration of more aggressive management, such as starting screening at younger ages, performing screenings more frequently, and additional risk-reduction strategies.[21]	NA	NA
	Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness.[21]	Individualized	NA
	Clinical encounter, including clinical breast exam, ongoing risk assessment and risk-reduction counseling[21]	25 years, or 5 to 10 years younger than the earliest age of breast cancer diagnosis in the family	Every 6 to 12 months
	Mammogram[21]	Age 40, or modified to a younger age based on the family history of breast cancer	Annually
	Consider breast MRI with and without contrast.[21]	30 to 35 years, or modified to a younger age based on the family history of breast cancer	Annually
	Consider additional risk-reduction strategies.[21, 22]	Individualized	NA
Male Breast	Currently there are no specific medical management guidelines for male breast cancer risk in mutation carriers. However, the increase in risk warrants consideration of options for male breast cancer screening, such as patient breast awareness education and clinical breast examinations.[21, 22]	Individualized	NA
Prostate	Consider prostate cancer screening with digital rectal examination (DRE) and prostate specific antigen (PSA).[21, 23]	40 years	Every 1-2 years, or adjusted based on PSA
For Patients With A Cancer Diagnosis	For patients with a gene mutation and a diagnosis of cancer, targeted therapies may be available as a treatment option for certain tumor types (e.g., PARP-inhibitors).[24]	NA	NA

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the CHEK2 Biallelic gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

Since this patient has mutations in both copies of the *CHEK2* gene, it is almost certain that each of their parents and all of their children carry a *CHEK2* mutation. Siblings are at very high risk for carrying either one or two *CHEK2* mutations. Since even a single *CHEK2* mutation can lead to a significantly increased risk for cancer, it is especially important that this information be shared within the family and relatives talk with a healthcare provider about testing.

The children of this patient are at risk of inheriting two *CHEK2* mutations only if the other parent is also a carrier of a *CHEK2* mutation. Screening the other biological parent of any children for *CHEK2* mutations may be appropriate.

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